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PATENT  
Docket No. JCLA9793  
page 1

**UNITED STATE PATENT AND TRADEMARK OFFICE**

In re application of :  
Application No. : 10/660,139  
Filed : September 10, 2003  
For : METHOD OF FORMING BIOCHIP AND  
APPLICATION THEREOF  
  
Examiner : LUM, LEON YUN BON  
Art Unit : 1641

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October 28, 2005

(Date)

  
Jiawei Huang, Reg. No. 43,330

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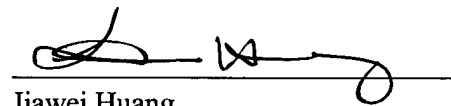
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**PATENT**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

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**EX PARTE HSU et al.**

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**Application for Patent**

**Filed September 10, 2003**

**Serial No. 10/660,139**

**FOR:  
METHOD OF FORMING BIOCHIP AND  
APPLICATION THEREOF**

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**APPEAL BRIEF**

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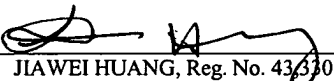
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JIAWEI HUANG, Reg. No. 43,330

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Representatives for Applicants

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I. REAL PARTY IN INTEREST

The real parties in interest are Jing-hsiang Hsu, Wen-Yih Chen, Rong-Seng Chang, Rong-Nan Huang, and Wen-Ren Li, the inventors named in the subject application, and National Central University, Taiwan, the assignee of record.

II. RELATED APPEALS AND INTERFERENCES

There are no related appeals and/or interferences.

III. Status of the Claims

A total of 4 claims were presented during prosecution of this application. Applicant appeals rejected claims 1 and 3-5.

IV. Status of the Amendments

Applicant did not file any Amendments after Final Rejection.

V. Summary of the Claimed Subject Matter

The claimed invention relates to a fabrication method for a biochip for a rapid detection of the biological activity of a peptide and the antigen-antibody interaction. The fabrication method comprises: providing a micro-carrier labeled with an identification code (Paragraph [0025] on page 6); covering the surface of the micro-carrier with a silicon dioxide layer (Paragraph [0026] on page 6) and chemically reacting the surface of the silicon dioxide layer with 3-aminopropyltriethoxysilane to modify the surface of the silicon dioxide layer into an aminated surface (Paragraphs [0037] and [0039] on page 7); and performing a solid-phase peptide synthesis step to synthesize a peptide with a specific amino acid sequence on

the aminated surface of the silicon dioxide layer (Paragraphs [0042] to [0047] on page 9). The material for forming the micro-carrier can be a high molecular weight material, such as polyethylene terephthalate (PET).

#### VI. Grounds of Rejection to Be Reviewed on Appeal

- A. Claims 1 and 5 were rejected under 35 U.S.C. 103(a) as being unpatentable over Nova et al. (US 5,872,214, hereinafter Nova) in view of Cozzette et al.(US 5,063,081, hereafter Cozzette).
- B. Claims 3-4 were rejected under 35 U.S.C. 103(a) as being unpatentable over Nova et al. in view of Cozzette et al., as applied to claim 1 above, and further in view of Wu et al. (US 5,922,161, hereinafter Wu).

#### VII. Arguments

##### A. The related law

A prima facie case of obviousness requires that the reference teachings “appear to have suggested the claimed subject matter.” *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143, 147 (CCPA 1976). To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

When more than one reference or source of prior art is required in establishing the obviousness rejection, “it is necessary to ascertain whether the prior art teachings would appear to be sufficient to one of ordinary skill in the art to suggest making the claimed substitution or other modification.” *In re Lalu*, 747 F.2d 703, 223 USPQ 1257, 1258 (Fed. Cir. 1984). There must be some motivation to combine the references; this motivation must come from “the nature of the problem to be solved, the teachings of the prior art, [or] the knowledge of persons of ordinary skill in the art.” *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998).

Finally, if an independent claim is nonobvious under 35 U.S.C. 103 (or unanticipated under 35 U.S.C. 102), then any claim depending therefrom is nonobvious (or unanticipated). *In re Fine*, 837 F.2d 1071, 5 USPQ2d, 1596 (Fed. Cir. 1988).

B. Claims 1 and 5 were improperly rejected under 35 U.S.C. 103(a) as being unpatentable over Nova et al. (US 5,872,214, hereinafter Nova) in view of Cozzette et al. (US 5,063,081, hereafter Cozzette).

The Examiner rejected claims 1 and 5 as being unpatentable over Nova in view of Cozzette. The Examiner indicated that Nova substantially teaches the method recited in claims 1 and 5, except that Nova fails to teach that the surface modification procedure comprises covering the surface of the micro-carrier with a silicon dioxide layer and reacting the silicon dioxide layer with 3-aminopropyltriethoxysilane. Cozzette is cited to cure the deficiencies of Nova. The Examiner stated that Cozzette discloses a biosensor wherein a silicon substrate is layered with silicon dioxide and further modified with 3-aminopropyltriethoxysilane.

Applicant respectfully disagrees with the Office's assertion that Nova in view of Cozzette shows all the limitations of the instant invention as defined in claim 1. Applicant believes Nova in view of Cozzette is legally deficient for the purpose of rendering claim 1 unpatentable.

Claim 1 recites a fabrication method for a biochip comprising: "providing a micro-carrier labeled with an identification code; covering a surface of the micro-carrier with a silicon dioxide layer and reacting a surface of the silicon dioxide layer with 3-aminopropyltriethoxysilane to modify the surface of the silicon dioxide layer into an aminated surface; and performing a solid-phase synthesis step to synthesize a peptide with a specific amino acid sequence on the aminated surface of the silicon dioxide layer". In other words, the silicon dioxide layer on the micro-carrier is chemically reacted with 3-aminopropyltriethoxysilane to convert the surface of the silicon dioxide layer into an aminated surface. Thereafter, the amine group on the carrier is chemically attached to an amino acid via a peptide bond with the carboxyl end of the amino acid. After several repetitions of the synthesis step, a plurality of amino acids can be sequentially attached to the micro-carrier to form a peptide that has a specific amino acid sequence. Accordingly, the micro-carrier with the peptide of a specific amino acid sequence can be used to identify the test-pending material.

Nova teaches, in very general terms, the concept of immobilizing biomolecules onto solid or liquid supports. As recognized by the Examiner, Nova is

completely silent about covering the surface of the micro-carrier with a silicon dioxide layer and reacting the silicon dioxide layer with 3-aminopropyltriethoxysilane. In addition, Nova also fails to teach or suggest synthesizing a peptide with a specific amino acid sequence on the aminated surface of a silicon dioxide layer. However, the Office Action contends that Cozzette cures the deficiencies of Nova. Applicant respectfully disagrees.

Cozzette substantially teaches a substrate (20), a non-conductive layer of silicon dioxide (15) disposed on the substrate (20), a patterned titanium metal structure (10) disposed on the silicon dioxide (15), an iridium electrocatalyst layer (5) disposed on the patterned titanium metal structure (10), a permselective silane layer (6) disposed on the iridium electrocatalyst layer (5) and a biolayer layer (7) disposed on a portion of the permselective silane layer (6) which is formed above the iridium electrocatalyst layer (5).

First of all, although a portion of the permselective silane layer (6) is disposed over the silicon dioxide layer (15) as shown in Fig. 2, the permselective silane layer (6) is mainly formed on the iridium electrocatalyst layer (5) by means of physical phenomena, such as coating or dispensing on the titanium metal layer (col. 28, ln. 9-11). There is no teaching or suggestion in Cozzette that the permselective silane reacts with the silicon dioxide. Although, Fig. 2 shows a minor portion of the permselective silane layer (6) is disposed on the silicon dioxide layer (15), Cozzette is completely silent about reacting and converting the surface of the silicon dioxide layer into an aminated surface. Further, in addition to promoting adhesion of the biolayer (7) to the underlying electrode surface (5), the permselective silane mainly functions as a molecular weight-sensitive transmissive film for excluding certain molecules from entering and diffusing through such a film (col. 14 ln. 49 to col. 15, ln. 67). Therefore, the permselective silane of Cozzette is directed to dispose between the biolayer (7) and the underlying electrode surface instead of on the silicon dioxide layer. Cozzette never expressly teaches to react the surface of a silicon dioxide layer with 3-aminopropyl-triethoxysilane. Accordingly, the Office Action's assertion that Cozzette provides the teaching or suggestion of modifying a silicon dioxide layer with 3-aminopropyl-triethoxysilane is unsubstantiated.

Secondly, the Office Action asserted that the biolayer (7) of Cozzette in Figure 2 can include polypeptides, which indicates that the 3-aminopropyltriethoxysilane modified silicon dioxide layer is capable of retaining polypeptides (pg 8-9 of the OA). However, in

Figure 2, Cozzette teaches forming the biolayer (7) over the part of the permselective silane (6) that is disposed above the iridium electrocatalyst layer (5) and not above the silicon dioxide layer (15). There is no contact between the biolayer (7) and the silicon dioxide layer (15). Therefore, even if the silicon dioxide layer (15) of Cozzette is modified with 3-aminopropyltriethoxysilane and even if the biolayer (7) of Cozzette is capable of retaining polypeptide, Cozzette still fails to teach synthesizing a peptide with a specific amino acid sequence on the aminated surface of the silicon dioxide layer because the biolayer (7) of Cozzette and bioactive molecules therein are not chemically attached to or on the silane-modified surface of the silicon dioxide layer, let alone the fact the silicon dioxide layer (15) of Cozzette is not reacted with 3-aminopropyltriethoxysilane.

Accordingly, the combination of Nova and Cozzette, in a manner suggested by the Examiner, cannot possibly render every features of claim 1 obvious. Therefore claim 1 and its dependent claim 5 patentably define over Nova and Cozzette and should be allowed.

- C. Claims 3-4 were improperly rejected under 35 U.S.C. 103(a) as being unpatentable over Nova et al. in view of Cozzette et al., as applied to claim 1 above, and further in view of Wu et al. (US 5,922,161, hereinafter Wu).

The Examiner rejected claims 3-4 as being unpatentable over Nova et al. in view of Cozzette et al., as applied to claim 1 above, and further in view of Wu et al. The Office Action acknowledged that “Nova et al and Cozzette et al references fail to teach that a material for forming the micro-carrier is a high molecular weight material or comprises polyethylene terephthalate (PET)”. Page 5, the last paragraph of the Office Action. The Examiner cited Wu to teach the polymeric material of ultra high molecular weight polyethylene and polyethylene terephthalate.

However, first of all, Wu cannot cure the above discussed deficiencies of Nova and Cozzette. Thus, for at least the same reasons discussed above, claims 1 as well as its dependent claims 3-4 are patentable over Nova, Cozzette and Wu.

Secondly, applicant traverses the proposed combination of Nova and Cozzette with Wu because of the lack of required suggestion and motivation. Wu teaches a method of modifying or tailoring the surface of polymers and or polymer-based materials to control surface and interface chemistry and molecular structure, including oxidizing the surface and



treating the oxidized surface with amine-containing organic compound. Abstract. The polymers of Wu include polyethylene terephthalate (PET). However, Wu never teaches or even remotely suggests covering the surface of the polymer or polyethylene terephthalate (PET) with a silicon dioxide layer. Instead, Wu requires that the surface be oxidized. Col. 4, lines 13-23. There is no suggestion or motivation to combine Wu with Nova and Cozzette as proposed by the Examiner. Applicant acknowledges that neither high molecular weight materials nor polyethylene terephthalate (PET) are new. But, covering the surface of these materials with silicon dioxide layer as recited in claims 3 and 4 is not taught or suggested by the cited references. Therefore, claims 3 and 4 are patentable over Nova, Cozzette and Wu.

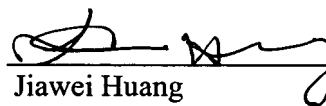
#### VIII. Conclusion

In view of the above discussion, Applicant believes that the rejections under 35 U.S.C. 103 are in error, and respectfully requests the Board of Patent Appeals and Interferences to reverse the Examiner's rejections of the claims on appeal.

Date: 10/28/2005

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Respectfully submitted,  
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## APPENDIX A - CLAIMS ON APPEAL

1. (previously presented) A fabrication method for a biochip, comprising:  
providing a micro-carrier labeled with an identification code;  
covering a surface of the micro-carrier with a silicon dioxide layer and reacting a surface of the silicon dioxide layer with 3-aminopropyltriethoxysilane to modify the surface of the silicon dioxide layer into an aminated surface; and  
performing a solid-phase peptide synthesis step to synthesize a peptide with a specific amino acid sequence on the aminated surface of the silicon dioxide layer.

Claim 2. (canceled)

3. (original) The method of claim 1, wherein a material for forming the micro-carrier is a high molecular weight material.

4. (original) The method of claim 1, wherein a material for forming the micro-carrier comprises polyethylene terephthalate (PET).

5. (original) The method of claim 1, wherein the identification code on the micro-carrier is a bar code or a number code.

Claims 6-16 (canceled)